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110> Yu et al. 🔭

- <120> Methods of Treatment of Immune System Related Disorders Using Neutrokine-alpha
- <130> PF343P3C4
- <150> 09/589,285
- <151> 2000-06-08
- <150> 09/507,968
- <151> 2000-02-22
- <150> 60/122,388
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	ccaa	acctt	ca a	aagtt	caaç	gt ag	gtgat									g cag ı Gln	173
	tca Ser 10	Arg	Leu	Thr	tct Ser	Cys	Leu	Lys	Lys	Arg	Glu	Glu	Met	Lys	Leu	Lys	221
,					atc Ile 30												269
					aag Lys												317
					acg Thr												365
					agc Ser												413

Chi Chi

461

aag ctg cca gca gga gca gga gcc ccc aag gcc ggc ctg gag gaa gct Lys Leu Pro Ala Gly Ala Gly Ala Pro Lys Ala Gly Leu Glu Glu Ala

90	`				95					100					105	
							aaa Lys									509
							agc Ser									557
							gac Asp 145									605
_							gga Gly									653
							gcc Ala									701
_	-		_				ttt Phe					_	_			749
							gga Gly									797
	_			_	-	_	agt Ser 225	_			_		_	_		845
		_		_			ccc Pro				_			_		893
							gat Asp									941
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_		ctg Leu	_	tgad	cctad	ett a	acaco	catgt	c to	gtago	ctatt	tto	cctc	cctt		1041

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1100

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und >

<212> PRT

<213> Homo sapiens

Met Ser Thr Glu Ser Met Ile Arg Asp Val Glu Leu Ala Glu Glu Ala Leu Pro Lys Lys Thr Gly Gly Pro Gln Gly Ser Arg Arg Cys Leu Phe Leu Ser Leu Phe Ser Phe Leu Ile Val Ala Gly Ala Thr Thr Leu Phe Cys Leu Leu His Phe Gly Val Ile Gly Pro Gln Arg Glu Glu Phe Pro Arg Asp Leu Ser Leu Ile Ser Pro Leu Ala Gln Ala Val Arg Ser Ser Ser Arg Thr Pro Ser Asp Lys Pro Val Ala His Val Val Ala Asn Pro 90 Gln Ala Glu Gly Gln Leu Gln Trp Leu Asn Arg Arg Ala Asn Ala Leu Leu Ala Asn Gly Val Glu Leu Arg Asp Asn Gln Leu Val Val Pro Ser 120 Glu Gly Leu Tyr Leu Ile Tyr Ser Gln Val Leu Phe Lys Gly Gln Gly 135 Cys Pro Ser Thr His Val Leu Leu Thr His Thr Ile Ser Arg Ile Ala 150 155 Val Ser Tyr Gln Thr Lys Val Asn Leu Leu Ser Ala Ile Lys Ser Pro 170 Cys Gln Arg Glu Thr Pro Glu Gly Ala Glu Ala Lys Pro Trp Tyr Glu Pro Ile Tyr Leu Gly Gly Val Phe Gln Leu Glu Lys Gly Asp Arg Leu Ser Ala Glu Ile Asn Arg Pro Asp Tyr Leu Asp Phe Ala Glu Ser Gly Gln Val Tyr Phe Gly Ile Ile Ala Leu

land cont

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Leu His Leu Leu Leu Gly Leu Leu Leu Val Leu Leu Pro Gly Ala 20 25 30

Gln Gly Leu Pro Gly Val Gly Leu Thr Pro Ser Ala Ala Gln Thr Ala 35 40 45 Arg Gln His Pro Lys Met His Leu Ala His Ser Thr Leu Lys Pro Ala 50 55 60

Ala His Leu Ile Gly Asp Pro Ser Lys Gln Asn Ser Leu Leu Trp Arg 65 70 75 80

Ala Asn Thr Asp Arg Ala Phe Leu Gln Asp Gly Phe Ser Leu Ser Asn 85 90 95

Asn Ser Leu Leu Val Pro Thr Ser Gly Ile Tyr Phe Val Tyr Ser Gln
100 105 110

Val Val Phe Ser Gly Lys Ala Tyr Ser Pro Lys Ala Thr Ser Ser Pro 115 120 125

Leu Tyr Leu Ala His Glu Val Gln Leu Phe Ser Ser Gln Tyr Pro Phe 130 135 140

His Val Pro Leu Leu Ser Ser Gln Lys Met Val Tyr Pro Gly Leu Gln 145 150 155 160

Glu Pro Trp Leu His Ser Met Tyr His Gly Ala Ala Phe Gln Leu Thr 165 170 175

Gln Gly Asp Gln Leu Ser Thr His Thr Asp Gly Ile Pro His Leu Val 180 185 190

Leu Ser Pro Ser Thr Val Phe Phe Gly Ala Phe Ala Leu 195 200 205

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1 5 10 15

Gly Ser Leu Leu Ala Val Ala Gly Ala Thr Ser Leu Val Thr Leu 20 25 30

Leu Leu Ala Val Pro Ile Thr Val Leu Ala Val Leu Ala Leu Val Pro
35 40 45

Gln Asp Gln Gly Gly Leu Val Thr Glu Thr Ala Asp Pro Gly Ala Gln
50 55 60

Ala Gln Gln Gly Leu Gly Phe Gln Lys Leu Pro Glu Glu Glu Pro Glu 65 70 75 80

Thr Asp Leu Ser Pro Gly Leu Pro Ala Ala His Leu Ile Gly Ala Pro

Leu Lys Gly Gln Gly Leu Gly Trp Glu Thr Thr Lys Glu Gln Ala Phe
100 105 110

Leu Thr Ser Gly Thr Gln Phe Ser Asp Ala Glu Gly Leu Ala Leu Pro

July Ch

115 120 125

Gln Asp Gly Leu Tyr Tyr Leu Tyr Cys Leu Val Gly Tyr Arg Gly Arg 130 135 140

Ala Pro Pro Gly Gly Gly Asp Pro Gln Gly Arg Ser Val Thr Leu Arg 145 150 155 160

Ser Ser Leu Tyr Arg Ala Gly Gly Ala Tyr Gly Pro Gly Thr Pro Glu 165 170 175

Leu Leu Glu Gly Ala Glu Thr Val Thr Pro Val Leu Asp Pro Ala 180 185 190

Arg Arg Gln Gly Tyr Gly Pro Leu Trp Tyr Thr Ser Val Gly Phe Gly
195 200 205

Gly Leu Val Gln Leu Arg Arg Gly Glu Arg Val Tyr Val Asn Ile Ser 210 215 220

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Val Met Val Gly

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Ser Ser Ala Ser Ser Pro Trp Ala Pro Pro Gly Thr Val Leu Pro Cys 20 25 30

Pro Thr Ser Val Pro Arg Arg Pro Gly Gln Arg Arg Pro Pro Pro 35 40 45

Pro Pro Pro Pro Pro Leu Pro Pro Pro Pro Pro Pro Pro Pro Leu Pro 50 55 60

Pro Leu Pro Leu Pro Pro Leu Lys Lys Arg Gly Asn His Ser Thr Gly 65 70 75 80

Leu Cys Leu Leu Val Met Phe Phe Met Val Leu Val Ala Leu Val Gly
85 90 95

Leu Gly Leu Gly Met Phe Gln Leu Phe His Leu Gln Lys Glu Leu Ala 100 105 110

Glu Leu Arg Glu Ser Thr Ser Gln Met His Thr Ala Ser Ser Leu Glu . 115 120 125

-7-

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Lys Gln Ile Gly His Pro Ser Pro Pro Pro Glu Lys Lys Glu Leu Arg
Lys Val Ala His Leu Thr Gly Lys Ser Asn Ser Arg Ser Met Pro Leu
Glu Trp Glu Asp Thr Tyr Gly Ile Val Leu Leu Ser Gly Val Lys Tyr
                                    170
Lys Lys Gly Gly Leu Val Ile Asn Glu Thr Gly Leu Tyr Phe Val Tyr
Ser Lys Val Tyr Phe Arg Gly Gln Ser Cys Asn Asn Leu Pro Leu Ser
                            200
His Lys Val Tyr Met Arg Asn Ser Lys Tyr Pro Gln Asp Leu Val Met
Met Glu Gly Lys Met Met Ser Tyr Cys Thr Thr Gly Gln Met Trp Ala
                    230
                                        235
Arg Ser Ser Tyr Leu Gly Ala Val Phe Asn Leu Thr Ser Ala Asp His
                         250
Leu Tyr Val Asn Val Ser Glu Leu Ser Leu Val Asn Phe Glu Glu Ser
                                265
Gln Thr Phe Phe Gly Leu Tyr Lys Leu
       275
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aacacannnn ncaggaaata atccattccc tgtggtcact tattctaaag gccccaacct 120
tcaaagttca agtagtgata tggatgactc cacagaaagg gagcagtcac gccttacttc 180
ttgccttaag aaaagagaag aaatgaaact gnaaggagtg tgtttccatc ctcccacgga 240
aggaaagccc ctctntccga tcctccaaag acggaaagct gctggctgca accttgntgn 300
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-10-

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-11-

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agtotggtga ctttgtttcg atgtattcaa aatatgcctg aaacactacc caataattcc 180
tgctattcag ctggcattgc aaaactggna ggaaggagat gaactccaac ttgcaatacc 240
aggggaaaat gcacaattat cactgggatg gagatgttca cattttttgg gtgccattga 300
aactgetgtg acctnettae aneangtget gttngetatt ttneetneet nttetntggt 360
aacctettag gaaggaagga ttettaaetg ggaaataaee caaaaaaann ttaaangggt 420
angngnnana ngnggggnng ttnncnngnn gnnttttngg nntatnttnt nntngggnnn 480
ngtaaaaatg gggccnangg gggnttttt
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<222> (213)

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ccgttcaggg tccagaagaa acagtcactc aagactgctt gcaactgntt gcagacagtg 180
aaacaccaac tatacaaaaa ggctcccttc tgntgccaca tttgggccaa ggaatggaga 240
gatttetteg tetggaaaca ttttgccaaa etetteagat aetetttnet etetgggaat 300
caaaggaaaa tototaotta gattnacaca tttgttocca tgggtntott aagttttaaa 360
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ncnntctttt gggntga
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<223> primer
<400> 11
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                                                                   33
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                                                                   26
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ctggggctgc tcctggtgtt gcctgctgcc ttccctgccc cagttgtgag acaaggggac 120
                                                                    129
ctggccagc
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aag aaa aga gaa gaa atg aaa ctg aag gag tgt gtt tcc atc ctc cca
                                                                   96
Lys Lys Arg Glu Glu Met Lys Leu Lys Glu Cys Val Ser Ile Leu Pro
cgg aag gaa agc ccc tct gtc cga tcc tcc aaa gac gga aag ctg ctg
Arg Lys Glu Ser Pro Ser Val Arg Ser Ser Lys Asp Gly Lys Leu Leu
get gea acc ttg ctg ctg gea ctg ctg tet tgc tgc ctc acg gtg gtg
                                                                   192
Ala Ala Thr Leu Leu Leu Ala Leu Leu Ser Cys Cys Leu Thr Val Val
     50
                         55
tet tte tae cag gtg gee gee etg caa ggg gae etg gee age ete egg
                                                                   240
Ser Phe Tyr Gln Val Ala Ala Leu Gln Gly Asp Leu Ala Ser Leu Arg
 65
                     70
gca gag ctg cag ggc cac cac gcg gag aag ctg cca gca gga gca gga
Ala Glu Leu Gln Gly His His Ala Glu Lys Leu Pro Ala Gly Ala Gly
                 85
gcc ccc aag gcc ggc ctg gag gaa gct cca gct gtc acc gcg gga ctg
                                                                   336
Ala Pro Lys Ala Gly Leu Glu Glu Ala Pro Ala Val Thr Ala Gly Leu
            100
aaa atc ttt gaa cca cca gct cca gga gaa ggc aac tcc agt cag aac
                                                                   384
Lys Ile Phe Glu Pro Pro Ala Pro Gly Glu Gly Asn Ser Ser Gln Asn
        115
age aga aat aag egt gee gtt eag ggt eea gaa gaa aca gga tet tae
                                                                   432
Ser Arg Asn Lys Arg Ala Val Gln Gly Pro Glu Glu Thr Gly Ser Tyr
    130
                        135
aca ttt gtt cca tgg ctt ctc agc ttt aaa agg gga agt gcc cta gaa
                                                                   480
Thr Phe Val Pro Trp Leu Leu Ser Phe Lys Arg Gly Ser Ala Leu Glu
145
                    150
                                         155
gaa aaa gag aat aaa ata ttg gtc aaa gaa act ggt tac ttt ttt ata
                                                                   528
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Glu																
	Lys	Glu	Asn	Lys 165	Ile	Leu	Val	Lys	Glu 170	Thr	Gly	Tyr	Phe	Phe 175	Ile	
														cat His		576
														ctg Leu		624
	_		_	_				_		_				aat Asn		672
														gaa Glu		720
														gga Gly 255		768
					gca Ala					tgad	cctad	ett a	acaco	catgt	cc	818
tgta	agcta	att t	tcct	ccct	t to	ctctc	gtaco	c tct	aaga	aaga	aaga	aatct	aa o	ctgaa	aaatac	878
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115 120 125

Ser Arg Asn Lys Arg Ala Val Gln Gly Pro Glu Glu Thr Gly Ser Tyr 130 135 140

Thr Phe Val Pro Trp Leu Leu Ser Phe Lys Arg Gly Ser Ala Leu Glu 145 150 155 160

Glu Lys Glu Asn Lys Ile Leu Val Lys Glu Thr Gly Tyr Phe Phe Ile 165 170 175

Tyr Gly Gln Val Leu Tyr Thr Asp Lys Thr Tyr Ala Met Gly His Leu 180 185 190

Ile Gln Arg Lys Lys Val His Val Phe Gly Asp Glu Leu Ser Leu Val 195 200 205

Thr Leu Phe Arg Cys Ile Gln Asn Met Pro Glu Thr Leu Pro Asn Asn 210 215 220

Ser Cys Tyr Ser Ala Gly Ile Ala Lys Leu Glu Glu Gly Asp Glu Leu 225 230 235 240

Gln Leu Ala Ile Pro Arg Glu Asn Ala Gln Ile Ser Leu Asp Gly Asp 245 250 255

Val Thr Phe Phe Gly Ala Leu Lys Leu Leu 260 265

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<213> Homo sapiens

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Ser Asp Val Thr Glu Val Met Trp Gln Pro Ala Leu Arg Arg Gly Arg 20 25 30

Gly Leu Gln Ala Gln Gly Tyr Gly Val Arg Ile Gln Asp Ala Gly Val 35 40 45

Tyr Leu Leu Tyr Ser Gln Val Leu Phe Gln Asp Val Thr Phe Thr Met 50 55 60

Gly Gln Val Val Ser Arg Glu Gly Gln Gly Arg Gln Glu Thr Leu Phe 65 70 75 80

Arg Cys Ile Arg Ser Met Pro Ser His Pro Asp Arg Ala Tyr Asn Ser 85 90 95

Cys Tyr Ser Ala Gly Val Phe His Leu His Gln Gly Asp Ile Leu Ser

Val Ile Ile Pro Arg Ala Arg Ala Lys Leu Asn Leu Ser Pro His Gly 115 120 125

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384

aat too tgo tac tog got ggc atc gcg agg ctg gaa gaa gga gat gag

Asn Ser Cys Tyr Ser Ala Gly Ile Ala Arg Leu Glu Glu Gly Asp Glu 120 115 att cag ctt gca att cct cgg gag aat gca cag att tca cgc aac gga Ile Gln Leu Ala Ile Pro Arg Glu Asn Ala Gln Ile Ser Arg Asn Gly 135 gac gac acc ttc ttt ggt gcc cta aaa ctg ctg taa ctcacttgct 478 Asp Asp Thr Phe Phe Gly Ala Leu Lys Leu Leu 150 ggagtgcgtg atccccttcc ctcgtcttct ctgtacctcc gagggagaaa cagacgactg 538 gaaaaactaa aagatgggga aagccgtcag cgaaagtttt ctcgtgaccc gttgaatctg 598 atccaaacca ggaaatataa cagacagcca caaccgaagt gtgccatgtg agttatgaga 658 aacggagccc gcgctcagaa agaccggatg aggaagaccg ttttctccaq tcctttqcca 718 acacgcaccg caaccttgct ttttgccttg ggtgacacat gttcagaatg cagggagatt 778 tccttgtttt gcgatttgcc atgagaagag ggcccacaac tgcaggtcac tgaagcattc 838 acgctaagtc tcaggattta ctctcccttc tcatgctaag tacacacacg ctcttttcca 898 ggtaatacta tgggatacta tggaaaggtt gtttgttttt aaatctagaa gtcttgaact 958 ggcaatagac aaaaatcctt ataaattcaa gtgtaaaata aacttaatta aaaaggttta 1018 agtgtgaaaa aaaaaaaaa aa 1040

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<212> PRT

<213> Homo sapiens

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Lys Ala Gly Leu Gly Glu Ala Pro Ala Val Thr Ala Gly Leu Lys Ile
Phe Glu Pro Pro Ala Pro Gly Glu Gly Asn Ser Ser Gln Ser Ser Arg
Asn Lys Arg Ala Ile Gln Gly Ala Glu Glu Thr Val Ile Gln Asp Cys
Leu Gln Leu Ile Ala Asp Ser Glu Thr Pro Thr Ile Gln Lys Gly Ser
                                     90
Tyr Thr Phe Val Pro Trp Leu Leu Ser Phe Lys Arg Gly Ser Ala Leu
Glu Glu Lys Glu Asn Lys Ile Leu Val Lys Glu Thr Gly Tyr Phe Phe
                            120
Ile Tyr Gly Gln Val Leu Tyr Thr Asp Lys Thr Tyr Ala Met Gly His
Leu Ile Gln Arg Lys Lys Val His Val Phe Gly Asp Glu Leu Ser Leu
                                        155
Val Thr Leu Phe Arg Cys Ile Gln Asn Met Pro Glu Thr Leu Pro Asn
                165
Asn Ser Cys Tyr Ser Ala Gly Ile Ala Lys Leu Glu Glu Gly Asp Glu
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Asp Val Thr Phe Phe Gly Ala Leu Lys Leu Leu
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gccatgggac atctaattca gaggaaaaaa gtccatgtct ttggggatga attgagtctg 480 gtgactttgt ttcgatgtat tcaaaatatg cctgaaacac tacccaataa ttcctgctat 540 tcagctggca ttgcaaaact ggaagaaggg gatgaacttc aacttgcaat accacgagaa 600 aatgcacaaa tatcactgga tggagatgtc acattttttg gtgccctcaa actgctg 657

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<212> PRT

2127 1101

<213> Homo sapiens

<400> 30

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20 25 30

Lys Ala Gly Leu Gly Glu Ala Pro Ala Val Thr Ala Gly Leu Lys Ile 35 40 45

Phe Glu Pro Pro Ala Pro Gly Glu Gly Asn Ser Ser Gln Ser Ser Arg 50 55 60

Asn Lys Arg Ala Ile Gln Gly Ala Glu Glu Thr Val Ile Gln Asp Cys 65 70 75 80

Leu Gln Leu Ile Ala Asp Ser Glu Thr Pro Thr Ile Gln Lys Gly Ser 85 90 95

Tyr Thr Phe Val Pro Trp Leu Leu Ser Phe Lys Arg Gly Ser Ala Leu 100 105 110

Glu Glu Lys Glu Asn Lys Ile Leu Val Lys Glu Thr Gly Tyr Phe Phe 115 120 125

Ile Tyr Gly Gln Val Leu Tyr Thr Asp Lys Thr Tyr Ala Met Gly His 130 135 140

Leu Ile Gln Arg Lys Lys Val His Val Phe Gly Asp Glu Leu Ser Leu 145 150 155 160

Val Thr Leu Phe Arg Cys Ile Gln Asn Met Pro Glu Thr Leu Pro Asn 165 170 175

Asn Ser Cys Tyr Ser Ala Gly Ile Ala Lys Leu Glu Glu Gly Asp Glu 180 185 190

Leu Gln Leu Ala Ile Pro Arg Glu Asn Ala Gln Ile Ser Leu Asp Gly
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Asp Val Thr Phe Phe Gly Ala Leu Lys Leu Leu 210 215

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gggatctgca gggatggaag gctgctggct gctaccctcc tgctggccct gttgtccagc 180
agtttcacag cgatgtcctt gtaccagttg gctgccttgc aagcagacct gatgaacctg 240
cgcatggagc tgcagagcta ccgaggttca gcaacaccag ccgccgcggg tgctccagag 300
ttgaccgctg gagtcaaact cctgacaccg gcagctcctc gaccccacaa ctccagccgc 360
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tcagctcctc ctgcaccatg cctgcctgga tgccgccatt ctcaacatga tgataatgga 480
atgaacctca gaaacatcat tcaagactgt ctgcagctga ttgcagacag cgacacgccg 540
gccttggagg agaaagagaa caaaatagtg gtgaggcaaa caggctattt cttcatctac 600
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Cut.

agccaggttc tatacacgga ccccatcttt gctatgggtc atgtcatcca gaggaagaaa 660

gtacacgtct ttggggacga gctgagcctg gtgaccctgt tccgatgtat tcagaatatg 720 cccaaaacac tgcccaacaa ttcctgctac tcggctggca tcgcgaggct ggaagaagga 780 gatgagattc agcttgcaat tcctcgggag aatgcacaga tttcacgcaa cggagacgac 840 accttctttg gtgccctaaa actgct

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<211> 289

<212> PRT

<213> Mus musculus

<400> 38

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Ser Glu Lys Gly Glu Asp Met Lys Val Gly Tyr Asp Pro Ile Thr Pro 20 25 30

Gln Lys Glu Glu Gly Ala Trp Phe Gly Ile Cys Arg Asp Gly Arg Leu 35 40 45

Leu Ala Ala Thr Leu Leu Leu Ala Leu Leu Ser Ser Ser Phe Thr Ala 50 55 60

Met Ser Leu Tyr Gln Leu Ala Ala Leu Gln Ala Asp Leu Met Asn Leu 65 70 75 80

Arg Met Glu Leu Gln Ser Tyr Arg Gly Ser Ala Thr Pro Ala Ala Ala 85 90 95

Gly Ala Pro Glu Leu Thr Ala Gly Val Lys Leu Leu Thr Pro Ala Ala 100 105 110

Pro Arg Pro His Asn Ser Ser Arg Gly His Arg Asn Arg Arg Ala Phe 115 120 125

Gln Gly Pro Glu Glu Thr Glu Gln Asp Val Asp Leu Ser Ala Pro Pro 130 135 140

Ala Pro Cys Leu Pro Gly Cys Arg His Ser Gln His Asp Asp Asn Gly
145 150 155 160

Met Asn Leu Arg Asn Ile Ile Gln Asp Cys Leu Gln Leu Ile Ala Asp 165 170 175

Ser Asp Thr Pro Ala Leu Glu Glu Lys Glu Asn Lys Ile Val Val Arg 180 185 190

Gln Thr Gly Tyr Phe Phe Ile Tyr Ser Gln Val Leu Tyr Thr Asp Pro 195 200 205

Ile Phe Ala Met Gly His Val Ile Gln Arg Lys Lys Val His Val Phe 210 215 220

Gly Asp Glu Leu Ser Leu Val Thr Leu Phe Arg Cys Ile Gln Asn Met 225 230 235 240

Pro Lys Thr Leu Pro Asn Asn Ser Cys Tyr Ser Ala Gly Ile Ala Arg 245 250 255

CINT

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Gln Ile Ser Arg Asn Gly Asp Asp Thr Phe Phe Gly Ala Leu Lys Leu
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